REMARKS

The present invention is directed to methods of treatment of a nonspecified *Candida* species isolate using antimycotic delivery systems. These systems are suitable for use in the vaginal cavity. The invention is additionally concerned with methods utilizing preparations demonstrating a controlled, extended or sustained release of the active and/or therapeutic agent and a minimal number of administrations to produce efficacy upon administration of said delivery system. The methods and systems are especially effective against *Candida* species causing vaginal irritation, and thus reduce the need for identification of the isolate prior to treatment.

Upon entry of the forgoing amendments, claims 1-27 are pending in the application. Claims 17, 19, 22 and 24 have been amended to clarify the language contained therein. The amendments do not add any new matter within the meaning of 35 U.S.C. §132. Accordingly, entry of the amendments to the claims as noted above is respectfully requested.

CLAIM OBJECTIONS

Claims 17 and 19 are objected to for incorporating language, which does not recite an active step. Applicants thank the Examiner for his suggestions in this regard and have amended the claims accordingly.

As such, Applicants request that the Examiner reconsider and withdraw this objection to claims 17 and 19.

REJECTION UNDER 35 U.S.C. §112, SECOND PARAGRAPH

Claims 9-16, 19, 20, 21 and 24-27 are rejected under 35 U.S.C. §112, second paragraph as being indefinite.

Applicants traverse this rejection in light of the amendment of Claim 24 for purposes of clarity.

For example, claim 9 is directed to a method of treatment of "an **unidentified** vulvovaginal fungal condition...wherein the condition is caused by a *Candida* species selected from the group consisting of *dubliniensis*, *tropicalis*, *glabrata*, *parapsilosis*, *krusei*, and *lusitaniae*." Emphasis added. In the text of the rejection, the Examiner states that it is unclear "how a method of treatment of an **undiagnosable** vulvovaginal condition can comprise

treating a condition caused by a species of *Candida*, which must have been diagnosed in order for it to be known." Emphasis added.

Applicants submit that identification and diagnosis are not the same within the context of the instant subject matter. Specifically, a doctor may culture a sample when a patient complains of vulvovaginal symptoms to identify the infective agent(s). The infective agent(s) may thus be "identified" through a culture or "unidentified" if not cultured. However, often times in the case of vulvovaginal conditions, such as a fungal infection, a doctor may **diagnose** the condition based on the patient's presented symptoms, rather than through actual **identification** of the specific infective agent(s). Thus, one can have an **unidentified** infective agent as the cause of a **diagnosed** condition. For this reason, Claim 24 has been amended to further clarify the significant differences between the terms "diagnosed" or "undiagnosed" with those of "identified" or "unidentified".

As now amended, each of claims 9-16, 19-21, and 24-27 is drawn to a method of treating a condition of **unidentified** specific origin, rather than an **undiagnosed** condition.

Accordingly, Applicants respectfully request the Examiner to reconsider and withdraw the rejection of claims 9 -16, 19-21 and

24-27 under 35 U.S.C. §112, second paragraph.

REJECTION UNDER 35 U.S.C. §102(b):

Claims 9 and 24-27 stand rejected under 35 U.S.C.§102(b) as being anticipated by Brown, et al., *Journal of Reproductive Medicine*, in view of Stedman's Medical Dictionary ("Brown" and "Stedman's", respectively).

Applicants respectfully traverse the rejection of claims 9 and 24-27 under 35 U.S.C.§102(b). A *prima facie* case of anticipation with respect to Brown in view of Stedman's has not been established for the reasons set forth below.

Brown is directed to a comparison of the safety and efficacy of a single vaginal dose of butoconazole nitrate 2% sustained release cream with that of a seven day schedule of miconazole nitrate 2% vaginal cream in the treatment of vulvovaginal candidias caused by *C. albicans*. See, Objective, Introduction, Patient Selection, and Results: Microbiological Cure Rate sections. Although Brown teaches that of the 150 known species of Candida, only nine are pathogenic in humans, which are *albicans, glabrata, tropicalis, pseudotropicalis, lusitaniae, crusei, rugosa, parapsilosis and guilliermondi*, it does not follow that the Brown treatments for *C. albicans* would be effective against the other

eight species named. Accordingly, Brown does not teach the use of the *C. albicans* treatments with respect to the other *Candida* species nor does it teach of efficacy for the treatments with respect to the other *Candida* species.

Stedman's medical dictionary defines "cream" as a semisolid emulsion of either the oil-in-water or the water-in-oil type, ordinarily intended for topical use.

In contrast, the present invention is directed to methods of treatment of nonspecified *Candida* isolates, specifically, the non-*albicans Candida* species *C. dubliniensis*, *C. tropicalis*, *C. glabrata*, *C. parapsilosis*, *C. krusei*, and *C. lusitaniae*, using antimycotic delivery systems. The methods of the present invention differ from the teachings of Brown in that the methods of the present invention are not directed to the treatment of *C. albicans* as is Brown whether using a cream or not.

Accordingly, the present subject matter differs significantly from the teachings of the cited references. For these reasons, in addition to others not set forth herein, the rejection of claims 9 and 24-27 under 35 U.S.C.§102(b) is inappropriate. Reconsideration and withdrawal of the rejection is respectfully requested.

REJECTION UNDER 35 U.S.C. §103(a):

Claims 1-27 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Riley in U.S. Patent No. 5,266,329 (the '329 patent), in view of Brown, *supra,* and Garg in *Pharmaceutical Tech. Drug Delivery* ("Garg"), and Droegemueller et al. in *Obstet. Gynecol* ("Droegemueller").

Applicants respectfully traverse the rejection of claims 1-35 under 35 U.S.C. §103(a). A *prima facie* case of obviousness has not been established with respect to the '329 patent, in view of Brown and Garg and Droegemueller for the reasons set forth below.

To establish a *prima facie* case of obviousness by combining prior art references, a suggestion or motivation for combining the teachings to make the invention "must be founded in the prior art, not in the applicant's disclosure." In re Dow Chem., 837 F2d 469, 473, 5 USPQ2d 1529, 1531 (Fed. Cir. 1988).

The '329 patent teaches systems which release an active agent in a controlled manner for an extended period in a vaginal cavity environment. When the systems incorporate an antifungal agent, i.e. an imidazole, the conventional treatment time may be reduced by at least 25%. Specifically, the '329 patent teaches that the conventional treatment period or quantity of agent used is reduced by at least 25%, whereas normally a controlled release drug system reduces the number of times a day that a drug must be administered

rather than the overall length of treatment. See, col. 4, lines 5-20. The `329 patent teaches that tests utilizing imidazoles upon *C. albicans* have demonstrated this result.

Brown teaches only treatments for *C. albicans*.

Garg teaches suitable excipients for use in vaginal formulations.

Droegemueller teaches that one dose of 2% butoconazole nitrate vaginal cream results in a maximum plasma level 24 hours after dosing.

To the contrary, the present invention is directed to methods of treatment of nonspecified non-*albicans Candida* isolates, specifically, the *Candida* species *C. dubliniensis*, *C. tropicalis*, *C. glabrata*, *C. parapsilosis*, *C. krusei*, and *C. lusitaniae*, using antimycotic delivery systems.

Applicants submit that one of skill in the art would not look to the teachings of the `329 patent, in view of Brown, Garg and Droegemueller unless doing so on the basis of the impermissible hindsight gained from the teachings of the instant specification. Particularly, this is true since the secondary references provide no motivation to combine their teachings in light of the teachings of the `329 patent. However, even if one were to rely on hindsight and combine the `329, Brown, Garg and Droegemueller references, it would still not make obvious each and every limitation of the subject invention as claimed, i.e., methods of treating

nonspecified *Candida* isolates, specifically, the *Candida* species *C. dubliniensis*, *C. tropicalis*, *C. glabrata*, *C. parapsilosis*, *C. krusei*, and *C. lusitaniae*, using antimycotic delivery systems.

For these reasons, in addition to others not noted herein, the rejection of claims 1-27 under 35 U.S.C. §103(a) as being unpatentable over the '329 patent, in view of Brown and Garg and Droegemueller is inappropriate. Reconsideration and withdrawal of the rejection of claims 1-27 is respectfully requested.

CONCLUSION

In view of the foregoing, Applicants earnestly request the Examiner reconsider and withdraw the outstanding rejections. The Examiner is invited to contact the undersigned attorney if it is believed that such contact will expedite the prosecution of the application.

Respectfully submitted,

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